

WO 2005/078105 A2

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
25 August 2005 (25.08.2005)

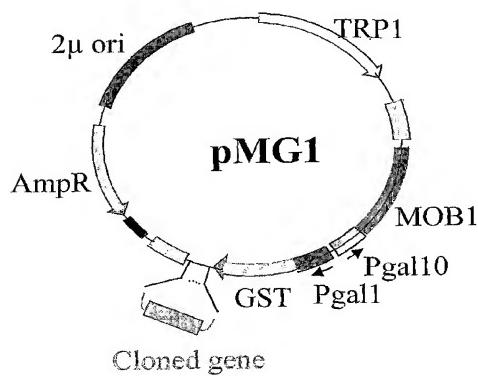
PCT

(10) International Publication Number
WO 2005/078105 A2

- (51) International Patent Classification⁷: **C12N 15/63** Institute for Medical Research, The Ridgeway, Mill Hill, London, NW7 1AA (GB).
- (21) International Application Number: PCT/GB2005/000372 (74) Agents: **MARSHALL, Cameron, John_ et al.**; Carpmaels & Ransford, 43-45 Bloomsbury Square, London WC1A 2RA (GB).
- (22) International Filing Date: 4 February 2005 (04.02.2005)
- (25) Filing Language: English (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (26) Publication Language: English
- (30) Priority Data: 0402660.5 6 February 2004 (06.02.2004) GB (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO,
- (71) Applicant (for all designated States except US): **MEDICAL RESEARCH COUNCIL [GB/GB]**; 20 Park Crescent, London W1B 1AL (GB).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): **SEDGWICK, Steven [GB/GB]**; The National Institute for Medical Research, The Ridgeway, Mill Hill, London, NW7 1AA (GB). **GEYMONAT, Marco [IT/GB]**; The National

[Continued on next page]

(54) Title: SELECTION MARKERS USEFUL FOR HETEROLOGOUS PROTEIN EXPRESSION



(57) Abstract: Selection markers in prior art systems are based on resistance genes or on complementation of auxotrophic mutations. The requirement for expression of these markers is conditional e.g. on the presence of an antibiotic, or on the absence of a nutrient. In contrast, the selection markers used in this invention are non-conditional, and selection pressure is absolute. The markers involved are genes which encode essential survival factors, such that loss of the marker gene is lethal. Thus the invention provides a cell which expresses chromosomal genes and extra-chromosomal genes, wherein (a) the expressed extra-chromosomal genes include an essential gene whose expression is unconditionally required for survival of the cell, (b) the expressed chromosomal genes do not include said essential gene, and (c) the extra-chromosomal genes include a heterologous gene. The cells can conveniently be obtained by a plasmid shuffling procedure.



SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN,
GQ, GW, ML, MR, NE, SN, TD, TG).

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